REMARKS

The October 2, 2009 Official Action and the reference cited therein have been carefully reviewed. In view of the following remarks, favorable reconsideration and allowance of this application are respectfully requested.

At the outset, it is noted that a shortened statutory response period of three (3) months was set forth in the October 2, 2009, Official Action. Therefore, the initial due date for response is January 2, 2009. Attached hereto is a petition for a one month extension of time as the response is being filed within the one month extension period.

As a preliminary matter, Applicants note that the request for continued examination has been entered. Thus, the finality of the previous Official Action has been withdrawn. Accordingly, claims 1-2, 7, 10, 13-14, 39-41 and 43-45 have been examined on the merits, and claims 3-6, 8-9, 11-12, 15-30, 38, and 42 remain withdrawn from consideration.

Turning to the substantive aspects of the October 2, 2009, Official Action, the Examiner has rejected claims 1-2, 7, 10, 13-14, 39-41 and 43-45 under 35 U.S.C. §103(a) as allegedly being unpatentable over Rovinski et al. (of record) and Esslinger et al. (J. Clin. Invest. (2003) 111:1673-1681), asserting that this new grounds of rejection was necessitated by Applicants' previous amendments to the claims.

The foregoing constitutes the entirety of the rejections raised in the October 2, 2009, Official Action. Applicants respectfully submit that the claims as instantly presented are patentable, and therefore, are in condition for allowance.

CLAIMS 1-2, 7, 10, 13-14, 39-41 and 43-45 ARE PATENTABLE OVER ROVINSKI ET AL. AND ESSLINGER ET AL.

At page 2 of the Official Action, the Examiner has rejected claims 1-2, 7, 10, 13-14, 39-41 and 43-45, as allegedly being unpatentable over Rovinski et al., and Esslinger et al. It is the Examiner's position that Rovinski et al. teach a prime-boost method of inducing an antibody

response to HIV antigens, particularly envelope glycoprotein. In order to induce the immune response, Rovinski et al. disclose priming with plasmids encoding the envelope glycoprotein, and then boosting with non-infectious, non-replicating HIV-like particles that encode the envelope glycoprotein. The reference is also relied on for teaching that in creating VLPs, certain genes/proteins can be modified or obtained from different HIV isolates (for example, ENV from BX08 can be employed in VLPs and the GAG and POL genes of modified HIV can originate from the same or different isolates). The Examiner admits that Rovinski et al. do not teach the use of an infectious, non-replicating lentivirus, but relies on Esslinger et al. for disclosing use of an infectious, replication deficient lentivirus in a prime-boost method to determine if two administrations of the same vector/vaccine causes antivector immunity against the second administration. Notably, these investigators determined that such immunity was present. Surprisingly, in view of these teachings, the Examiner concludes that it would be obvious for a skilled artisan modify Rovinski et al. to use a lentivirus that is infectious but replication deficient in a heterologous prime-boost method given the teaching of Esslinger et al.

By way of background, the Examiner bears the burden of establishing a prima facie case of obviousness for each of the rejections appearing in the Office Action. In re Rijckaert, 28 U.S.P.Q.2d 1934, 1935 (Fed. Cir. 1993). To establish a prima facie case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to combine the references in a manner resulting in the claimed invention. M.P.E.P. §2143.01; In re Dow Chem. Co., 5 U.S.P.Q.2d 1929 (Fed. Cir. 1988). Second, a reasonable expectation of success must exist. M.P.E.P. §2143.02. Third, the prior art, taken alone or when combined, must teach or suggest each and every element recited in the claims.

M.P.E.P. §2143.03. Moreover, each of these requirements must "be found in the prior art, and not based on applicant's disclosure." M.P.E.P. §2143; In re Fritch, 23 U.S.P.Q.2d 1780 (Fed. Cir. 1992). Considering the foregoing, Applicants respectfully traverse the rejection for the following reasons.

Initially, Rovinski et al. emphasize that it is a crucial feature of the disclosure that the boost plasmids encoding the HIV-like particles (i.e., VLPs) are non-replicating and **non-infectious**. See, for example, page 3, paragraph 44 wherein it is taught : "[i]n a preferred aspect of the invention, the non-infectious, non-replicating immunogenic HIV-like particles may co-administered with the DNA construct in the priming administration and the DNA construct may be co-administered with the HIV-like particles in the boosting administration." It is not logical to conclude that skilled artisan would be motivated to modify the crucial feature of Rovinski et al. (i.e., non-infectious particle administration) since the procedure disclosed in the reference worked as intended. Applicant's are also unclear as to where the expectation of success can be found in the combination of Esslinger et al. with Rovinski et al. as detailed hereinbelow.

The Examiner relies on Esslinger et al. for teaching use of infectious, non-replicating constructs, (i.e., lentivectors) for use in T cell vaccines. The study concludes that in vivo administration of lentivector was better than transfer of transduced dendritic cells or peptide/adjuvant vaccination. Notably, the use of lentivector to elicit an immune response to an antigen in a prime-boost strategy was also investigated. Figure 5 demonstrates, and Esslinger et al. report that the second administration of the antigen containing vector, e.g., lentivector with antigen followed by lentivector with antigen, exhibited "similar kinetics and amplitude as seen during the primary administration", indicating that a prime-boost effect was not observed. In view of the results reported by Esslinger et al., it is unclear to Applicants how skilled artisans in this art area

would have been motivated to modify Rovinski et al. using the teachings of Esslinger et al. The skilled artisan would be unlikely to use the infectious lentivector strategy of Esslinger et al. in the method of Rovinski et al. in light of the lackluster results obtained in the prime-boost procedure that was disclosed. Although Rovinski et al. made it clear that it was preferable to use non-infectious lentiviruses, and Esslinger et al. use an infectious lentivector, neither of the references place an emphasis on the infectious nature of the construct to the extent that a skilled artisan would expect an improvement by replacing the non-infectious vector of Rovinski et al. with the infectious lentivector used in Esslinger et al. See also page 1680, left column, third full paragraph of Esslinger et al. which describes the difficulty in predicting whether prime-boost schemes work at all.

It appears that the Examiner employed impermissible hindsight reconstruction in combining the teachings of Rovinski et al. and Esslinger et al. to arrive at the instantly claimed invention. The Office has not provided a clear and particular showing of how the references would have motivated one of ordinary skill in the art to combine the teachings to arrive at the claimed invention based on the results in the references. In re Dembiczak, 50 U.S.P.Q.2d 1614 (Fed. Cir. 1999). The mere fact that references can be combined or modified **does not** render the resulting combination obvious unless the prior art also suggests the desirability of the combination. MPEP § 2143.01, citing In re Mills, 16 U.S.P.Q.2d 1430 (Fed. Cir. 1990). The Examiner appears to have taken Applicants' disclosure as a blueprint to defeat patentability, and the Examiner's conclusory statements at the middle of page 4 of the Official Action do not adequately address the issue of motivation to combine because the "factual question of motivation is material to patentability, and [cannot] be resolved on subjective belief and unknown authority." In re Lee, 277 F.3d 1338, 1343-44 (Fed. Cir. 2002). This lack of motivation to combine presents a

fundamental flaw in the instant rejection. In fact, following the Supreme Court's ruling in KSR Intn'l Co. v. Teleflex Inc., 2007 WL 1237837 (2007), the U.S.P.T.O. issued a memorandum instructing examiners that, in forming a rejection under §103(a), based upon a combination of prior art elements, "it remains necessary to identify the reason why a person of ordinary skill in the art would have combined the prior art elements in the manner claimed." See May 3, 2007 memo from M.A. Focarino, Deputy Commissioner for Patent Operations. In the present case, there is no objective evidence in the record supporting the Examiner's conclusory remarks regarding the alleged motivation to combine. Thus, as instructed by the court in KSR, the prior opinion in Graham v. John Deere Co., 383 U.S. 1 (1996), continues to define the inquiry and controls the non-obviousness analysis under §103; reaffirming the impermissibility of Examiners utilizing hindsight.

Inasmuch as the references cited by the Examiner fail to place the invention as claimed in the hands of the public, the rejection of the claims under §103 cannot be maintained. Accordingly, Applicants request that the rejection of the pending claims over Rovinski et al and Esslinger et al. be withdrawn.

CONCLUSION

In view of the amendments presented herewith and the foregoing remarks, it is respectfully urged that the objections and rejections set forth in the October 2, 2009, Official Action be withdrawn and that this application be passed to issue.

In the event the Examiner is not persuaded as to the allowability of any claim, and it appears that any outstanding issues may be resolved through a telephone interview, the

Examiner is requested to call the undersigned at the phone number given below.

Respectfully submitted,
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